Amendments to the Drawings

The attached replacement sheets of drawings, which include Figures 1A, 1B, 2A, 2B, 3A, 3B, 4A, 4B, 5A, 5B, 6, 7, 8, 9, 10, and 11, replace the original drawings. The replacement drawings are being submitted only for clarity. No changes have been made to the drawings.

Attachment: Replacement Sheets

Remarks

I. Status of the Claims

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 50-61 are pending in the application, with claim 50 being the independent claim. Claim 50 is sought to be amended. New claims 60 and 61 are sought to be added. Support for the amendment to claim 50 and new claims 60 and 61 may be found in the specification at page 17, lines 3-5 and 10-19. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

II. The Rejection Under 35 U.S.C. § 102(b) Is Traversed

In the Decision on Appeal dated July 18, 2007, the Board of Patent Appeals and Interferences (hereinafter "the Board") affirmed the rejection of claims 50-53 as being anticipated by Lee *et al.*, *Science 239*: 1288-1291 (1988) (hereinafter "Lee"). However, because the Board's reasoning differed from that of the Examiner, the Board designated the rejection as to claims 50-53 as being a new ground of rejection. Applicants respectfully traverse this rejection in view of the claims, as currently presented.

As an initial note, the Examiner in the final Office Action mailed July 20, 2005, the Advisory Action mailed December 5, 2005, and the Examiner's Answer mailed July 11, 2006, contended that Lee discloses the purification of porcine and murine tetrameric

uricases that contain 100% tetrameric uricase because Lee mentions that porcine and murine urate oxidase were "purified to homogeneity." *See* Lee at page 1289. The Examiner thus interpreted a "homogeneous" preparation of uricase in Lee to encompass a preparation in which 100% of the uricase is in the tetrameric form. *See* final Office Action mailed July 20, 2005 at pages 3-4, Advisory Action mailed December 5, 2005 at page 3 and Examiner's Answer mailed July 11, 2006 at page 9. Furthermore, the Examiner pointed to a statement in Lee that mammalian uricase "is associated with the peroxisome and exists as a tetramer with an apparent subunit size of 32,000 daltons" (*See* Lee at page 1288) to support his contention that the mammalian uricase disclosed in Lee was 100% in the tetrameric form. *See* final Office Action mailed July 20, 2005 at page 5, Advisory Action mailed December 5, 2005 at page 4 and Examiner's Answer mailed July 11, 2006 at page 5. Applicants respectfully disagreed (and still disagree) with these contentions. In the Decision on Appeal, the Board agreed with Applicants that the Examiner had taken the above statements out of context to support his contention. *See* Decision on Appeal at page 3. Thus, Applicants reiterate and incorporate herein their previous remarks concerning this contention by the Examiner, but are not further addressing this specific point in the present Amendment and Reply since the Board has effectively removed it as a basis for rejecting the pending claims.

With regard to the Board's Decision on Appeal, Applicants respectfully traverse this rejection in view of the claims, as currently presented. Claim 50 (and thus the claims depending therefrom) is directed to an isolated tetrameric mammalian uricase, wherein greater than 90% of the uricase is in a tetrameric form and less than 10% of the uricase is in a non-tetrameric aggregated form. Applicants respectfully assert that Lee

does not expressly disclose an isolated tetrameric mammalian uricase, wherein greater than 90% of the uricase is in a tetrameric form as required by the present claims. Lee only discloses a commercial preparation of porcine liver uricase from Sigma and a natural preparation of murine liver uricase. Lee does not indicate in *what* form the uricase preparations were in, let alone that greater than 90% of the uricase preparations were in a tetrameric form. Hence, Lee does not expressly disclose each and every element recited in the present claims.

In addition, Applicants respectfully assert that Lee does not inherently disclose an isolated tetrameric mammalian uricase, wherein greater than 90% of the uricase is in a tetrameric form as required by the present claims. To rely on an inherency argument, "the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic *necessarily* flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (PTO Bd. Pat. App. Int. 1990) (emphasis in original). This burden has not been met in the present case, since there is no disclosure in Lee, nor any sound scientific reasoning, that uricases containing greater than 90% tetrameric uricase "necessarily flow" from the disclosure in Lee.

As is clearly indicated in the present specification, prior to the present invention, isolated tetrameric uricase wherein greater than 90% of the uricase was in a tetrameric form had not been taught in the art. Prior to the present invention, isolated preparations of natural and recombinant uricase, including those disclosed in Lee, contained a *mixture* of forms of the enzyme, including a high content of non-tetrameric aggregates. *See* specification at page 16, lines 5-16. Indeed, the preparations used in Lee would not

contain uricase in which greater than 90% of the uricase was in a tetrameric form and less than 10% of the uricase was in a non-tetrameric aggregated form. *See* specification at page 16, lines 5-8.

This contention is further supported by Example 1 in the present specification which discloses that the commercial preparation of porcine liver uricase used in Lee (and also used as a starting material by the inventors of the present application) had to be purified by the methods described in the present application in order to obtain a preparation in which greater than 90% of the uricase was in the tetrameric form. *See* specification at page 20, lines 9-13. The present specification further discloses that natural and recombinant uricases isolated from bacteria, fungi, mammals and plants require purification by the methods described in the present specification in order to obtain an isolated tetrameric uricase preparation in which greater than 90% of the uricase was in the tetrameric form. *See* specification at Examples 4-10. Thus, the commercial preparation of porcine liver uricase and the natural preparation of murine liver uricase disclosed in Lee clearly would not have been expected to contain greater than 90% of the uricase in the tetrameric form.

This conclusion is further supported by the data presented in the accompanying Second Declaration Under 37 C.F.R. § 1.132 by Merry R. Sherman, Ph.D. (hereinafter "the second Sherman Declaration"). These data clearly show that the amount of uricase in the tetrameric form that is present in the commercial preparation of porcine liver uricase used both in Lee and as a starting material in the present invention was significantly lower than the "greater than 90%" required by the present claims. *See* paragraph 7 and Figure 3 of the second Sherman Declaration. As is shown in Figure 3,

and as stated by Dr. Sherman at paragraph 7, the Sigma porcine liver uricase (U3250) contained only about 62% tetramer prior to purification by the methods described in the present application. *See* Figure 3 and paragraph 7 of the second Sherman Declaration. Furthermore, these data show that the amount of uricase in the tetrameric form that is present in other isolated commercial, recombinant and natural uricase preparations was significantly lower than the "greater than 90%" required by the present claims. *See* paragraphs 8-11 and Figures 4 and 5 of the second Sherman Declaration. As is shown in Figures 4 and 5 and as stated by Dr. Sherman at paragraphs 8 and 10-11, the Sigma porcine liver uricase (Catalog No. U3377) contained only 86% tetramer; the soybean uricase contained only 65% tetramer; and the *Candida utilis* uricase (Sigma Catalog No. U1878) contained only 55% tetramer prior to purification by the methods described in the present application. *See* Figures 4 and 5 and paragraphs 8 and 10-11 of the second Sherman Declaration.

Indeed, as Dr. Sherman states at paragraphs 10 and 16 and as Figures 1, 2 and 5 clearly show, preparations of uricase that contain greater than 90% of the uricase in the tetrameric form could only be obtained by using the methods described in the present application, thereby resulting in the presently claimed uricase preparations. *See* Figures 1, 2, and 5 and paragraphs 10 and 16 of the second Sherman Declaration. Hence, as described in the present specification, and clearly shown in the accompanying second Sherman Declaration, without specifically purifying the uricase preparations using the methods disclosed in the present specification, the uricase preparations disclosed in Lee would not (and did not) contain greater than 90% tetrameric uricase. Thus, as one of ordinary skill in the art would readily appreciate, Lee does not disclose, either expressly

or inherently, an isolated tetrameric mammalian uricase having the characteristics recited in the present claims.

Under 35 U.S.C. § 102, a claim can only be anticipated if every element in the claim is expressly or inherently disclosed in a single prior art reference. *See Kalman v. Kimberly Clark Corp.*, 713 F.2d 760, 771 (Fed. Cir. 1983), *cert. denied*, 465 U.S. 1026 (1984). As indicated above, Lee does not expressly or inherently disclose every element of the presently claimed invention. Hence, under *Kalman*, this reference cannot support a rejection under 35 U.S.C. § 102(b). In view of the foregoing remarks, Applicants respectfully assert that Lee does not anticipate claims 50-53. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b) over Lee therefore are respectfully requested.

III. Obviousness Type Double-Patenting Rejection

In the Advisory Action dated December 5, 2005, the Examiner maintained the rejection of claims 50-59 under the judicially created doctrine of obviousness type double-patenting as being unpatentable over claims 1-30 of U.S Patent No. 6,783,965 (hereinafter "the '965 patent"). Applicants respectfully traverse this rejection. However, solely to advance prosecution, and not in acquiescence to the Examiner's rejection, Applicants submit herewith a Terminal Disclaimer under 37 C.F.R. § 1.321(c) over the '965 patent. Accordingly, this rejection has been overcome. Thus, Applicants respectfully request that the rejection be withdrawn.

IV. Other Matters

The amendment to the specification is being made solely to correct a typographical error. *See* the second Sherman Declaration at paragraph 5. Replacement drawings are being submitted solely for clarity. These changes are believed to introduce no new matter, and their entry is respectfully requested.

V. Conclusion

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the rejections and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Shannon A. Carroll

Shannon A. Carroll, Ph.D.
Attorney for Applicants
Registration No. 58,240

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1100 New York Avenue, N.W.
Washington, D.C. 20005-3934
(202) 371-2600
707067_1.DOC